Facile access to versatile functional groups from alcohol by single multifunctional reusable catalyst

Sourav Biswas[a], Kankana Mullick[a], Sheng-Yu Chen[a], Anton Gudz[a], David M. Carr[b], Carlos Mendoza[a], Alfredo M. Angeles-Boza[a], Steven L. Suib[a,*]

[a] Department of Chemistry, University of Connecticut, U-3060, 55 North Eagleville Rd., Storrs, CT 06269, USA
[b] Physical Electronics, 18725 Lake Drive East, Chanhassen, MN 55317, USA

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ABSTRACT

Tandem oxidation processes enabling one-pot multistep reactions received great attention as an efficient synthetic methodology for construction of complex molecules from simple substrates by a single operation. We report here tandem oxidative transformations of seven different functional groups (imine, imidazole, cyanide, amide, lactone, ester and olefin) from a single substrate (alcohol) by a single cesium promoted mesoporous manganese oxide catalyst (meso Cs/MnO$_x$). High conversions were obtained with a broad range of substrates including aliphatic long chain alcohols. The catalyst can be reused without any loss of catalytic activity. We also demonstrated a unique multiple esterification reaction from a single aliphatic alcohol under aerobic atmospheric conditions catalyzed by meso Cs/MnO$_x$.

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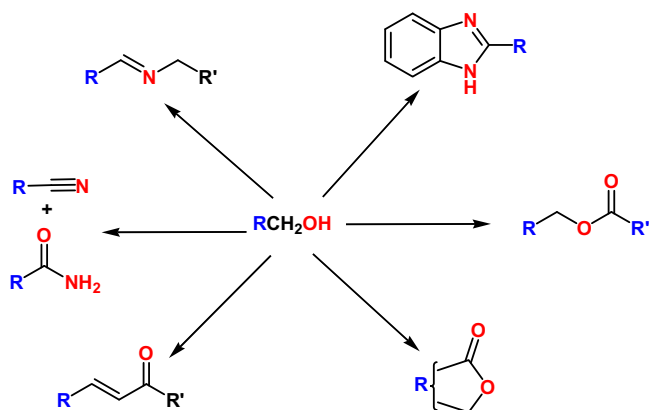
1. Introduction

Development of cleaner, safer and environmentally friendly technologies by using renewable feedstocks, reducing chemical wastes, and working with ecofriendly reagents has been stimulated by extensive research in past decades. To this end, tandem catalysis that enables 'one-pot' multistep reactions followed by a single work up step has drawn considerable attention from chemists [1–4]. 'One-pot' processes have several advantages: 1) operational simplicity due to a reduced number of steps; 2) significant time-cost benefits; 3) prevention of the isolation of volatile and toxic intermediates and 4) less waste generation [5]. Although several types of transition metal based catalysts have been introduced for tandem catalysis, most systems are homogeneous having shortcomings of product separations and catalyst reusability [6–8]. On the other hand, truly heterogeneous systems capable of performing tandem reactions with proper reusability have scarcely been reported [9–11]. Therefore, designing of a single cost-effective multifunctional heterogeneous catalyst for versatile tandem one-pot reactions from a single substrate is highly desirable.

Manganese oxide is a well-known heterogeneous catalyst for versatile catalytic oxidation reactions for its tunable redox properties, diverse crystal structures, and high abundance [12–14]. Manganese oxides as catalysts in 'tandem oxidation processes' (TOP) was first developed by establishing a synthetic route for the preparation of antibiotics, where a MnO$_2$ mediated oxidation combined with a Wittig olefination was performed [15]. In TOP, oxidation of alcohols is followed by trapping the intermediate aldehydes or ketones by nucleophilic reagents to form the desired product. Manganese oxide has also been utilized in TOP such as formation of imines, amides, quinoxalines, and terminal alkynes directly from alcohols [16–20]. However, manganese oxide mediated challenging tandem oxidative reactions involving three or more steps have not significantly been explored.

Nitrogen containing derivatives such as imines, imidazoles, cyanides and amides are key building blocks in the syntheses of natural products and biological compounds [21,22]. Regarding several strategies, one-pot TOP between alcohols and related nucleophiles are most acceptable, due to use of cheap and stable starting material (alcohol) [15,23,24]. However, the effective catalytic systems for one-pot TOP involve either precious metals, long reaction times, or have narrow applicability for a limited numbers of alcohols [25–28]. The other important aspect of TOP is to utilize commercially available alcohols in carbon–carbon bond formation, a fundamental reaction in organic synthesis. To this end, one pot metal catalyzed

Scheme 1. Versatile tandem oxidation process from alcohol by meso Cs/MnOx.

Fig. 1. (A) PXRD of meso Cs/MnOx at different calcination temperatures (250 °C, 350 °C, 450 °C and 550 °C).

oxidation/olefination of alcohols with ketones and Wittig reagents are two common technologies [29–33]. Other functionalities such as esters are widely used in fine chemicals, natural products, and fuel additives [34]. Among several methodologies, oxidative esterification of alcohols is a promising protocol in terms of green, economical, and sustainable chemistry. Nevertheless, most of the heterogeneous systems in this regard are based on noble metals (Au, Pd) and the assistance of basic promoters are inevitable to achieve high efficiency [35,36].

An inevitable linkage of mesoporous materials with heterogeneous catalysis has been recognized due to some intrinsic features such as high surface area, tunable porous structure, and ability to accommodate active nanosize metals on the surface [37,38]. Recently, we reported tunable soft templated mesoporous manganese oxide materials for catalytic oxidation reactions [39–42]. A minute amount (0.16%) of electropositive Cs$^+$ ions were introduced in the mesoporous manganese oxide (meso Cs/MnOx) as the structural promoter ions, which resulted enhanced catalytic activity in selective aerobic oxidation of alcohols to carbonyl groups, mesitylene to 3.5-dimethylbenzoic acid, and amines to imines. Herein, we document cesium ion promoted mesoporous manganese oxide (meso Cs/MnOx) material as a multifunctional catalyst for the transformation of alcohols to different functional moieties in one-pot tandem oxidative conditions. Seven different functional groups (imine, imidazole, cyanide, amide, lactone, ester and olefin) can be obtained starting from alcohols by the same catalyst (Scheme 1). The catalytic procedure described herein has the following advantages over the current systems for the tandem oxidation process: 1) a variety of commercially available alcohols can be used as the starting material; 2) reactions can be done mostly in aerobic atmospheric conditions; 3) inexpensive manganese oxide can be used as a catalyst instead of precious metal based systems and 4) products can be separated easily by simple filtration and the catalyst is reusable.

2. Experimental section

2.1. Synthesis of mesoporous Cs/MnOx

The catalyst was synthesized following the procedure described in the literature[39,40]. In a typical synthesis 0.02 mol of manganese nitrate tetrahydrate (Mn(NO$_3$)$_2$·4H$_2$O) and 0.134 mol of 1-butanol were added into a 120 mL beaker. To this solution 0.0034 mol of poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) (Pluoronic P123, PEO$_{20}$PPO$_{70}$PEO$_{20}$, molar mass 5750 g mol^{-1}) and 0.032 mol of concentrated nitric acid (HNO$_3$) were added and stirred at room temperature until the solution became clear (light pink). To this clear solution 200 μL of 1.0 M
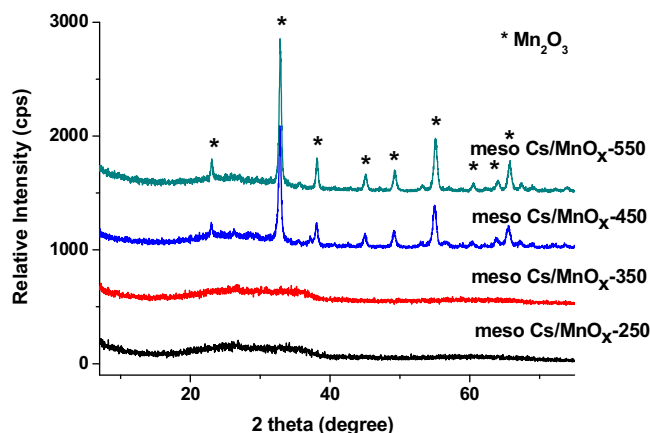
cesium nitrate (CsNO$_3$) aqueous solution was added maintaining the Cs loading to 1.0% with respect to Mn by mol (though ICP-MS revealed very low loading (0.16%) of Cs with respect to Mn [39]). The resulting clear solution was then kept in an oven at 120 °C for 3 h under air. The product was collected and washed with excess ethanol, centrifuged, and dried in a vacuum oven overnight. At the end, the dried black powders were subjected to a heating cycle. First they were heated at 150 °C for 12 h and cooled to room temperature under ambient conditions followed by a second heating step of 250 °C for 3 h.

2.2. Catalytic activity measurements

#### 2.2.1. Preparation of imines

In a 25 mL one necked round bottom flask equipped with a condenser, a mixture of alcohol (1.0 mmol), amine (2.0 mmol), catalyst (50 mg) and toluene (5.0 mL) was added. The reaction mixture was heated to reflux under vigorous stirring (700 rpm) for the required time under an air balloon. After reaction, the mixture was cooled and the catalyst was removed by filtration. The product analysis was done using GC–MS (gas chromatography-mass spectrometry). The conversion was determined based on the concentration of alcohols. Most reactions were repeated twice and the average values were used. For kinetic experiments, a two-necked flask was used where the other neck was used as a sampling port.

2.2.2. Preparation of benzimidazoles

In a 25 mL two necked round bottom flask equipped with a condenser, a mixture of alcohol (0.5 mmol), catalyst (50 mg) and toluene (5.0 mL) was added. The reaction mixture was heated to reflux under vigorous stirring (700 rpm) for the required time under an air balloon. The consumption of alcohol was monitored by GC–MS. After complete conversion of alcohol to aldehyde, *ortho*-phenyldiamine (1.0 mmol) was introduced in to the reaction mixture in order to scavenge the aldehyde. After reaction, the mixture was cooled and the catalyst was removed by filtration. The product analysis was done using GC–MS.

2.2.3. Preparation of α,β unsaturated ketone
2.2.3.1. Coupling of alcohol and Wittig reagent. A mixture of alcohol (0.5 mmol), Wittig reagent (1.0 mmol), catalyst (100 mg), and toluene (5.0 mL) was placed in a 25 mL round bottom flask equipped with a condenser. The reaction mixture was heated to reflux under vigorous stirring (700 rpm) for the required time under an air balloon. After reaction, the mixture was cooled and the catalyst was removed by filtration. The product analysis was done using GC–MS.
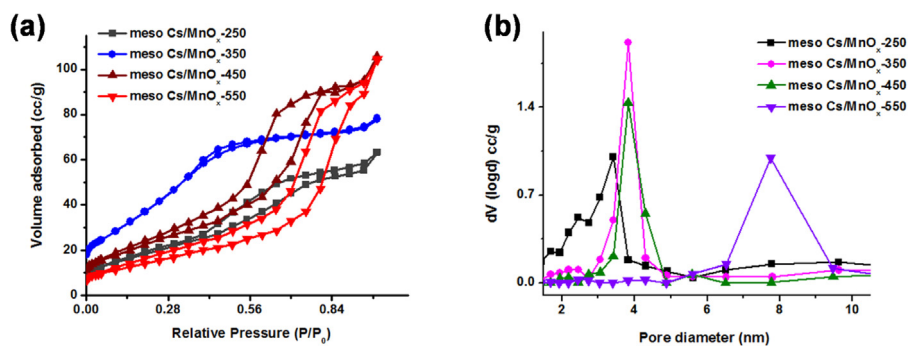
Fig. 2. (a) Nitrogen sorption isotherms and (b) BJH desorption pore size distribution of meso Cs/MnO$_x$ at different calcination temperatures (250 °C, 350 °C, 450 °C and 550 °C).

The conversion was determined based on the concentration of alcohol.

2.2.3.2. Coupling of acetophenone and benzyl alcohol. A mixture of benzyl alcohol (0.5 mmol), acetophenone (1.0 mmol), catalyst (100 mg), K$_2$CO$_3$ (1.5 mmol) and toluene (5.0 mL) was placed in a 25 mL round bottom flask equipped with a condenser. The reaction mixture was heated to reflux under vigorous stirring (700 rpm) for the required time under an air balloon. After reaction, the mixture was cooled and the catalyst was removed by filtration. The product analysis was done using GC–MS. The conversion was determined based on the concentration of benzyl alcohol.

2.2.3.3. Coupling of 1-phenylethanol and benzyl alcohol. A mixture of benzyl alcohol (0.5 mmol), 1-phenylethanol (1.0 mmol), catalyst (100 mg), K$_2$CO$_3$ (1.5 mmol) and toluene (5.0 mL) was placed in a 25 mL round bottom flask equipped with a condenser. The reaction mixture was heated to reflux under vigorous stirring (700 rpm) for the required time under an air balloon. After reaction, the mixture was cooled and the catalyst was removed by filtration. The product analysis was done using GC–MS. The conversion was determined based on the concentration of benzyl alcohol.

2.2.4. Preparation of amides
The oxidation experiments of alcohols to amide were carried out in a 100 mL cylindrical stainless steel pressurized reactor made by PARR Instrument Company, USA. The reactor was charged with a mixture of alcohol (0.5 mmol), catalyst (100 mg), acetonitrile (10 mL) and aqueous ammonia (28 wt%, 400 μL), followed by purging with oxygen and pressurized to 5 bar. The reactor was then heated to 130 °C for 15 h with constant stirring. After reaction, the reactor was cooled to room temperature and the catalyst was removed by filtration from the reaction mixture. The product analysis was done using GC–MS.

2.2.5. Preparation of esters
In a 25 mL two necked round bottom flask equipped with a condenser, a mixture of alcohol (4 mL), and catalyst (100 mg) was added. The reaction mixture was heated to reflux under vigorous stirring (700 rpm) for the required time under an air flow. After reaction, the mixture was cooled and the catalyst was removed by filtration. The product analysis was done using GC–MS. The conversion was determined based on the concentration of alcohols.

2.2.6. Preparation of lactones
In a 25 mL one necked round bottom flask equipped with a condenser, a mixture of diol (0.5 mmol), catalyst (50 mg) and toluene (5 mL) was added. The reaction mixture was heated to reflux under vigorous stirring (700 rpm) for 15 h under an air balloon. After reaction, the mixture was cooled and the catalyst was removed by

filtration. The product analysis was done using GC–MS. The conversion was determined based on the concentration of alcohol.

3. Results

3.1. Structural characterization of meso Cs/MnO$_x$

The material was synthesized by an inverse micelle templated evaporation induced self-assembly strategy as described for recently discovered University of Connecticut (UCT) mesoporous materials [43]. Powder X-ray diffraction measurements (Fig. 1) indicate the poorly crystalline nature of meso Cs/MnO$_x$ at low calcination temperatures (<350 °C) and crystalline bixbyite (Mn$_2$O$_3$) phase at higher temperatures (>400 °C). Type IV adsorption isotherms followed by Type I hysteresis loops (revealed form the nitrogen adsorption studies, Fig. 2a) confirm the mesoporous structure of the material irrespective of calcination temperature. The material possessed monomodal uniform pore size distributions and an increment of pore size was observed with the rising calcination temperature (Fig. 2b). The results are summarized in Table S1. The pore size increment is a typical characteristics of UCT material due to sintering of nanoparticles with heat treatment[43]. The scanning electron microscopy (SEM) images (Fig. S1) displayed arrogation of nanoparticles and development of pores are clearly observed in the material calcined at 550 °C.

The Mn 2p XPS spectra of the material at different calcination temperature have two peaks, which were assigned as Mn 2p$_{3/2}$ and Mn 2p$_{1/2}$ core levels (Fig. S2 and Table S2). The binding energies (641.7 ± 0.2) eV of Mn fall in the region of BEs of Mn^{3+} for all the materials irrespective of heating temperature[44]. No other oxidation states of Mn were detected. The O1 s spectra showed relatively broad peaks, which signify the presence of multiple oxygen species. The O 1 s region was further deconvoluted to three components corresponding to three different oxygen species [structural or lattice oxygen (O$_s$), surface adsorbed oxygen (O$_{ads}$) and adsorbed water or hydroxyl group (O$_{mw}$)] with distinct binding environments (Figs. S3 and S4). The relative amount of structural oxygen (O$_s$) was higher than the other type of oxygen species, which is typical for manganese oxide materials[44].

In this study, we focused on the meso Cs/MnO$_x$ material calcined at 250 °C. The surface area was calculated to be 79 m^2 g^{-1}, whereas the pore diameter was 3.4 nm. We used time-of-flight secondary ion mass spectrometry (TOF-SIMS) to determine the lateral and depth homogeneity of Cs ions on the manganese oxide surface. As revealed from Figs. S5 and S6 , the highest relative level of Cs is on the surface, however Cs also penetrated into the bulk. The presence of basic sites in the material due to Cs incorporation (by CO$_2$ adsorption experiments) was observed in our previous study, which was responsible for the enhanced activity compared to bare manganese oxide in oxidation of amines to imines[39].

Table 1
Tandem imine formation from alcohol by meso Cs/MnOx.[a]

$$R_1CH_2OH + R_2NH_2 \xrightarrow[\text{Toluene, 110}^\circ\text{C}]{\text{mesoCS/MnO}_x} R_1HC = NR_2$$

Entry	R$_1$	R$_2$	time (h)	Conv. (%)[b]	Selec. (%)[b,c]	TON[d]
1	Ph	n-butyl	2	>99	>99 (89)	3.3 (1111)
2	4-OMe-Ph	n-butyl	2	97	56	3.2(1078)
3	4-NO$_2$-Ph	n-butyl	2	90	75	3.0(1000)
4	2-thiophene	n-butyl	6	>99	94	3.3(1111)
5	cinnamyl	n-butyl	6	77	60	2.6(856)
6	2-napthalene	n-butyl	2	97	56	3.2(1078)
7[e]	2,4,6-trimethyl-Ph	n-butyl	8	90	75	3.0(1000)
8[e]	1-dodecanol	n-dodecyl	20	25	>99	0.8(222)
9	Ph	Ph	2	>99	>99 (87)	3.3(1111)
10	Ph	PhCH$_2$	2	>99	>99 (82)	3.3(1111)
11	Ph	4-NO$_2$-Ph-CH$_2$	15	40	80	1.3(444)
12	Ph	n-dodecyl	4	>99	>99	3.3(1111)

[a] Reaction Conditions: Alcohols (1.0 mmol), amines (2.0 mmol), catalyst (50 mg), toluene (5.0 mL), 110 °C, air balloon.
[b] Determined by GC–MS. Numbers in parenthesis refer to yields of isolated products.
[c] The other products were the corresponding aldehydes.
[d] TON = no of moles of alcohol converted per mole of catalyst (in parenthesis, TON was calculated based on Cs as active limiting sites).
[e] 100 mg catalyst were used.

3.2. One-pot imine formation

Initially, we focused on one-pot tandem imine formation from alcohols by meso Cs/MnOx under aerobic conditions. The imine products could be separated easily by basic alumina column chromatography using hexane and dichloromethane as solvent. The isolated yields of some of the imine derivatives are given in Table 1 along with their ^{1}H NMR and ^{13}C NMR data (see Supporting information). We first selected n-butylamine as a model nucleophile and reacted this with alcohols having diverse structures. As observed from Table 1, a reaction between benzyl alcohol and n-butylamine produced the corresponding imine with a very high conversion (>99%) and selectivity (>99%) [Table 1, Entry 1]. Whereas, benzyl alcohol with different functional groups (electron withdrawing and electron donating) reacted to the corresponding imines with excellent conversion (>99%) and moderate selectivity [Table 1, Entry 2 and 3]. The other products were the corresponding aldehydes. Meso Cs/MnOx displayed high conversion (>99%) and selectivity (94%) towards imine when 2-thiophenemethanol was used as the substrate [Table 1, Entry 4]. High activity (77% conversion, 60% selectivity) in tandem oxidation of an allylic alcohol (cinnamyl alcohol) [Table 1, Entry 5] revealed the superior chemo-selectivity nature of the meso Cs/MnOx, since no reaction at the double bond was identified by GC–MS. A bulky alcohol (2-napthylmethanol) was converted to the corresponding imine efficiently [Table 1, Entry 6]. The catalyst was also able to oxidize a sterically hindered alcohol to corresponding imine in high conversion (90%) [Table 1, Entry 7]. However, a longer reaction time (8 h) as well as higher amounts of catalyst (100 mg) were required. Furthermore, a reaction between an inactive long chain alcohol (1-dodecanol) and a long chain amine (n-dodecylamine) produced an imine bearing 24 carbon atoms with moderate conversion (20%) but excellent selectivity (>99%) [Table 1, Entry 8]. The catalyst also exhibited high conversions and selectivity when structurally different amines were selected as substrates [Table 1, Entry 9–12]. N-benzylideneaniline was produced with excellent selectivity (>99%) by a reaction between benzyl alcohol and aniline [Table 1, Entry 9]. Direct imine formation between benzyl amine and benzyl alcohol was observed with a very high conversion (>99%) and selectivity (>99%) [Table 1, Entry 10]. A very low conversion (40%) was achieved by selecting a weak nucleophilic amine (4-nitro benzylamine) [Table 1, Entry 11], whereas amines with a higher nucleophilic nature produced imines with excellent conversion (>99%) and selectivity (>99%) [Table 1, Entry 1 and 12].
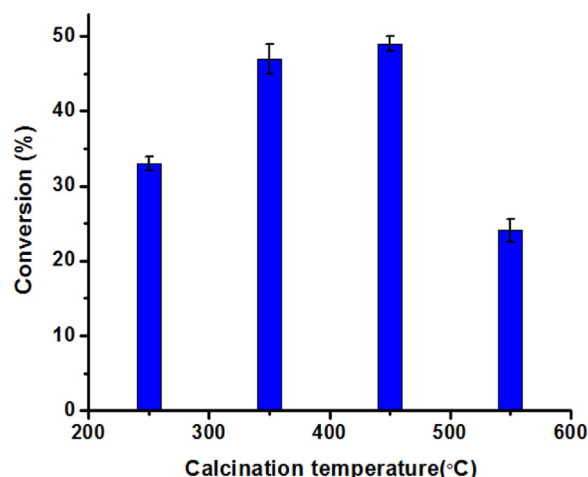
Fig. 3. Comparison of the activity of oxidation of benzyl alcohol and n-dodecylamine by meso Cs/MnOx at different calcination temperatures. Reaction condition: benzyl alcohol (1.0 mmol), n-dodecylamine (2.0 mmol), meso Cs/MnOx (25 mg), toluene (5 mL), 110 °C, 1 h, air balloon.
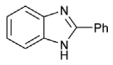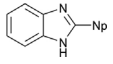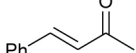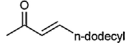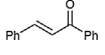
3.3. Kinetic and mechanistic study

To gain insight into the origin of the catalytic activity of meso Cs/MnOx, we have selected one-pot imine conversion of benzyl alcohol and n-dodecylamine as the model reaction. We first observed the oxidation of benzyl alcohol in absence of amine (Fig. S7). Next, a significant increase of conversion was achieved in the presence of amine, due to fast consumption of benzaldehyde (Fig. S7). Both these reactions depicted first order kinetics with respect to benzyl alcohol (Fig. S8 and S9). On the other hand, no significant difference in conversion was found in the direct condensation of benzaldehyde and n-dodecylamine in the presence of catalyst. We then selected a poorly nucleophilic amine (4-nitroaniline) and performed the condensatio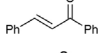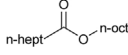n reaction in the presence of catalyst. Meso Cs/MnOx was found to expedite the condensation of benzaldehyde and 4-nitroaniline by 21% after 3 h of reaction (Table S3).

The catalytic activity of the material at different calcination temperature was compared, since calcination has a remarkable effect in the performance of UCT materials [40,41]. As revealed in Fig. 3, an increase of conversion was observed with the heat treatment from 250 °C to 350 °C. The material calcined at 450 °C displayed very similar performance to the material calcined at 350 °C. However, the

Table 2
Various tandem reactions from alcohols by meso Cs/MnOx.[a]

Entry	Alcohol	Amine	Product	Time (h)	GC yield[b] (%)
1[c]	PhCH₂OH	*(o-phenylenediamine)*	*(2-Ph-benzimidazole)*	15	50[d]
2[c]	NpCH₂OH	*(o-phenylenediamine)*	*(2-Np-benzimidazole)*	15	50[d]
3[e]	PhCH₂OH	NH₄OH	PhCONH₂	15	25[f]
4[e]	4OMe-PhCH₂OH	NH₄OH	4OMe-PhCONH₂	15	70[f]
5	PhCH₂OH	Ph₃P=CHC(O)CH₃	*(PhCH=CHC(O)CH₃)*	4	80[d]
6	n-dodecyl-OH	Ph₃P=CHC(O)CH₃	*(CH₃C(O)CH=CH-n-dodecyl)*	24	90[d]
7[g]	PhCH₂OH	PhCOCH₃	*(Ph-CH=CH-C(O)-Ph)*	36	80[d]
8[g]	PhCH₂OH	PhCHOHCH₃	*(Ph-CH=CH-C(O)-Ph)*	24	20[d]
9[h]	n-octyl-OH	N/A	*(n-hept-C(O)-O-n-oct)*	72	63[i]
10	*(benzene-1,2-dimethanol)*	N/A	*(phthalide)*	15	90[j]

[a] Reaction Conditions: Alcohols (0.5 mmol), tandem reagents (1.0 mmol), catalyst (50 mg), toluene (5.0 mL), 110 °C, air balloon.
[b] Determined by GC–MS based on alcohols as the limiting reagents.
[c] Diamine was added after full conversion of aldehydes.
[d] The other products were the corresponding aldehydes.
[e] Catalyst (100 mg), 400 μL NH₄OH, 5 bar of O₂, 130 °C, acetonitrile as solvent (10 mL).
[f] The other products were the corresponding cyanides.
[g] 1 eq of K₂CO₃ was used.
[h] 4 mL of 1-octanol, no solvent, under air flow.
[i] The other products were octyl octanoate (21%), and octyl hexanoate (16%).
[j] The other product was phthaldialdehyde.

activity decreased significantly when the material was heated to 550 °C. Calcination beyond 550 °C was not been performed, since the material becomes unstable and the mesoporous structure is destroyed.

3.4. Reusability and heterogeneity

Control experiments were then performed to verify the heterogeneous nature of the catalyst. We tested catalytic transformation of benzyl alcohol and *n*-dodecylamine under tandem oxidation conditions by meso Cs/MnOx. After the reaction, the catalyst was removed by filtration and the filtrate was tested by inductively coupled plasma (ICP) analysis. No Mn and Cs ions were detected by ICP and a minute change in Cs amount (0.04%) was observed in the used material. X-ray diffraction (XRD) analyses before and after use revealed no change of amorphous structure of the material (Fig. S10). Furthermore, the catalyst could be reused with the same catalytic performance for at least three times (Table S4). On the basis of these observations, we can conclude that our catalyst has truly heterogeneous nature, and is not only active but also has sustainability and reusability.

3.5. Benzimidazole formation

Excellent results in tandem imine formation encouraged us to explore the meso Cs/MnOx in more complex tandem oxidation processes. Benzimidazole derivatives are nitrogen containing cyclic compounds, which classically synthesized by coupling of *ortho*-phenyldiamine and carboxylic acid derivatives under acidic and harsh reaction condition [45]. The other method is oxidation of benzimidazoline intermediates generated by condensation

of *ortho*-phenyldiamine and aldehydes [46]. We utilized here the meso Cs/MnOx to synthesize benzimidazole derivatives by combining oxidation of alcohols to aldehydes followed by condensation with *ortho*-phenyldiamine with in tandem one-pot condition. In an initial attempt, no product was found when we use benzyl alcohol and *ortho*-phenyldiamine at the same time in reaction mixture. Therefore, we first conducted the oxidation of benzyl alcohol by the catalyst in presence of air at 110 °C. The diamine was incorporated after full conversion of benzyl alcohol to benzaldehyde to afford the desired benzimidazole compound. Using this sequential addition of diamine after full conversion of alcohol, the corresponding imidazole was formed with 50% selectivity after 15 h of reaction. The other product was the intermediate aldehyde. Both benzyl alcohol and 2-napthyl alcohol [Table 2, Entry 1 and 2] produced the corresponding imidazole under aerobic one-pot condition.

3.6. Oxidative amidation

Synthesis of amide and nitrile from primary alcohols and ammonia in the presence of O₂ is a challenge, since the catalyst can be deactivated in presence of ammonia and water. Mizuno et al. described an efficient method in this regard using manganese oxide based octahedral molecular sieves (OMS-2) catalysts [10,20]. Similarly in our case, primary amides and nitriles can be synthesized from primary alcohol and ammonia using meso Cs/MnOx. The reactions between benzyl alcohol and 4-methoxy benzyl alcohol with aqueous ammonia (28 wt%, 400 μL) under O₂ (5 atm) produced the corresponding amide and nitrile with excellent conversion (>99%) and high selectivity (25/75% and 70/30% selectivity of amide/nitrile respectively) [Table 2, Entry 3 and 4]. Among the tested solvents, acetonitrile emerged as the best one (Table S5), since most of

Table 3
Solvent free aerobic oxidation of 1-octanol by different catalysts.[a]

Entry	Catalyst	Conversion (%)	Selectivity (%)		
			I	II	III
1	no	0	nd	nd	nd
2	Comm Mn_2O_3	0	nd	nd	nd
3	K-OMS−2[b]	2	nd	50	25
4	Meso MnO_x	72	26	67	7
5	AMO	42	28	58	14
6	Meso Cs/MnO_x	>99	16	63	21

[a] Reaction condition: 1-octanol (4 mL), catalyst (100 mg), air flow, 130 °C, 72 h.
[b] The other product was 1-octanal. Nd = not detected.

the solvents were oxidized in present reaction condition. Meso Cs/MnO_x has several advantages in primary amide syntheses, such as, use of inexpensive manganese oxide, easy handling of aqueous ammonia, water as the only side product, and readily available alcohols as the starting reagents.

3.7. C-C bond formation

Despite wide commercial availability, alcohols are very sluggish in carbon–carbon bond forming reactions for poor leaving group ability of hydroxide ions. We have successfully employed three different strategies to develop a one pot oxidation/olefination reaction by meso Cs/MnO_x, applicable to aromatic as well as inactive aliphatic alcohols. The first strategy (one pot oxidation/Wittig reaction) is associated with oxidation of alcohols to aldehydes followed by in situ reaction of aldehydes with a stabilized Wittig reagent. Using an aromatic (benzyl alcohol) and an aliphatic (1-dodecanol) alcohol as substrates afforded quantitative conversion and high selectivity to the corresponding α,β unsaturated ketones by meso Cs/MnO_x [Table 2, Entry 5 and 6]. In the second strategy, benzaldehyde was trapped by a base mediated condensation reaction with a ketone (acetophenone) to produce the α,β unsaturated ketone with excellent selectivity (80%) [Table 2, Entry 7]. The cross coupling procedure was further improved by applying a third strategy, which was the direct oxidation of primary and secondary alcohols followed by a condensation of the in situ generated aldehyde and ketone with moderate (20%) selectivity to α,β unsaturated ketones [Table 2, Entry 8].

3.8. Oxidative multiple esterification

The meso Cs/MnO_x catalyst was also applied to one-pot synthesis of esters by oxidation of alcohols. Unlike other tandem oxidation reactions, addition of a second substrate was not required as the alcohol can itself act as the tandem substrate. We performed oxidation of an aliphatic alcohol (1-octanol) with meso Cs/MnO_x under aerobic conditions. Surprisingly, the reaction yielded three different esters (octyl octanoate (21%), octyl heptanoate (63%) and octyl hexanoate (16%)) [Table 2, Entry 9 and Fig. S11]. This synthetic strategy has several advantages such as long chain esters can be manufactured from single alcohol as the only reactant, no precious metal and additives are required, and the reaction can be performed under aerobic conditions. The oxidative esterification method was further extended for lactonization of diols [47,48]. 1,2-Benzenedimethanol was converted to the corresponding lactone with excellent conversion (90%) and selectivity (98%) using air as the terminal oxidant [Table 2, Entry 10].

3.9. Comparison with different catalysts

In order to determine the effectiveness of meso Cs/MnO_x over the conventional highly active manganese oxide based catalysts, a series of experiments was performed. We have selected a notoriously difficult reaction, the oxidation of an inactive long chain aliphatic alcohol (1-octanol) under aerobic and solvent free conditions as the model reaction. The reaction did not proceed at all in the absence of catalyst [Table 3, Entry 1]. Similar to catalyst free conditions, commercial nonporous Mn_2O_3 was totally inactive [Table 3, Entry 2] under the present reaction conditions. The state-of-the-art manganese oxide catalyst for oxidation reactions, K-OMS-2 [13], displayed very low activity under identical conditions [Table 3, Entry 3]. Using bare mesoporous manganese oxide (made by UCT method) [43] and amorphous manganese oxide (AMO) [49] as reference catalysts, much lower conversion was achieved [Table 3, Entry 4 and 5]. Meso Cs/MnO_x outperformed all other manganese oxide based catalysts in the oxidative esterification of 1-octanol [Table 3, Entry 6].

4. Discussion

Based on the catalytic results discussed above, the meso Cs/MnO_x material can be considered as an efficient catalyst for versatile tandem oxidation reactions. In general, imines are synthesized by two distinct reaction steps from alcohols. The first step involved oxidation of benzyl alcohol to the corresponding benzaldehyde. In the second step, the imine was formed by a nucleophilic condensation of amine with the in situ generated benzaldehyde. The mechanism of oxidation of alcohol by meso Cs/MnO_x was thoroughly investigated in our previous study, where the redox cycle of active manganese centers along with its labile lattice oxygen molecules have been found to be the dominant factors [40]. On the other hand, the condensation between aldehyde and amine are generally very facile due to good electrophilic properties of aldehyde and the nucleophilic nature of the amine. In our study, condensation reactions between benzaldehyde and n-dodecylamine did not require any catalytic assistance. However, synthesis of imines can be difficult when amines with poor nucleophilic nature are used as substrates. In those cases, catalysts with strong coordinating ability (Lewis acidic sites) with the carbonyl oxygen can increase the electrophilic nature of the aldehyde to accelerate the reaction rate [18]. The Mn^{3+} centers of meso Cs/MnO_x can act as coordinating sites in order to facilitate imine formation. This scenario is reinforced by the fact that the condensation between benzaldehyde and a weak nucleophilic amine (4-nitroaniline) was accelerated in the presence of meso Cs/MnO_x (Table S3).

The meso Cs/MnO_x material showed a reduction of catalytic activity at high calcination temperature (550 °C) (Fig. 3). An increase of pore size with rising calcination temperatures (Table S1, Fig. 2) was observed for the material. According to the mechanism of UCT materials, the aggregation of nanoparticle build the material, whereas the intra-particle voids are the reason for mesopore construction [43]. With heat treatment, the nanoparticles sinter to form bigger size nanoparticles. As a result, the intra-particle voids as well as pore size increase and surface area decreases. Smaller particle sizes and higher surface areas provide more surface defects, which can act as active sites [50,51]. Therefore, the lower catalytic activity (Fig. 3) of meso Cs/MnO_x-550 can be explained based on the decrease of surface area (53 $m^2\,g^{-1}$) at 550 °C.

The reaction mechanism of one-pot imine formation was then proposed based on the experimental findings and previous reports (Scheme S1). First, alcohols were oxidized to corresponding aldehydes in the presence of air, which was subsequently condensed with the amines to form imines catalyzed by coordinating sites of Mn^{3+} centers (for amines with poor nucleophilic nature). Notably, the slower reaction rate of alcohol oxidation (30% conversion in 15 min) than condensation (>99% conversion in 5 min) indicates that the initial oxidation of alcohol is the rate determining step.

The diversity of the one pot imine formation was also shown by broad substrate scope. We found that our methodology worked well for diverse aromatic and aliphatic alcohol/amine derivatives. The effectiveness of the catalyst was observed in reaction of heteroatom (S) containing substrate, where a high conversion (>99%) and selectivity (94%) were observed, though heteroatoms are known to poison transition metal center of catalyst [52]. The longer reaction time and higher catalyst amounts for a sterically hindered alcohol is likely due to difficult abstraction of the benzylic proton caused by the steric hindrance of three adjacent methyl groups. The nucleophilic property of the amine had a significant influence in the reaction. This is supported by the results of very less conversion (40%) of a weakly nucleophilic 4-nitrobenzylamine even after 15 h of reaction, whereas aliphatic amines (n-butylamine and n-dodecylamine) with high nucleophilic nature gave very high conversion (>99%) and selectivity within 4 h.

In case of one-pot benzimidazole formation, the reaction was controlled by sequential addition of diamine after full conversion of alcohols to aldehydes, as the reaction hardly proceeded when both alcohol and diamine were added at the same time. A competitive adsorption of alcohol and diamine in the porous catalyst may be the reason behind the reluctance of both reactants to react at the same time. Based on previous reports, the imidazole formation reaction was believed to be promoted by one pot multiple transformations over meso Cs/MnO_x, involving a manganese oxide assisted catalytic oxidation of alcohol to aldehyde, and an oxidative dehydrogenation of benzimidazoline derivatives generated from the condensation of ortho-phenylenediamine and aldehyde (Scheme S2) [27,53]. However, in our study the benzimidazoline intermediate has not been identified by GC–MS, which is due to the facile oxidation of C—N bonds of benzimidazoline by meso Cs/MnO_x. This is in agreement with our previous study, where the catalyst exhibited superior activity in oxidation of C—N bonds of amines to imines promoted by the Cs ion induced basicity of manganese oxide [39]. The multifunctional ability of meso Cs/MnO_x can also be seen from the oxidative amidation of primary alcohols, where four consecutive reactions have occurred in one-pot: (1) oxidation of alcohol to aldehyde, (2) condensation of aldehyde and ammonia to produce the aldimine intermediate, (3) oxidative dehydrogenation of aldimine to cyanide and (4) hydration of cyanide to amide [10,20]. Use of 5 bar of oxygen is required in this case, since the reaction did not proceed at all under reflux conditions and atmospheric pressure. Deactivation of the porous catalyst in the presence of water may be the reason behind this.

The catalyst can also perform one-pot oxidative esterification of aliphatic alcohols under aerobic atmospheric conditions without addition of any basic additives. In general, an esterification reaction involves proton extraction from alcohol and acid and thereby promoted by base [54]. The heterogeneous catalysts mediated oxidative esterification usually required presence of basic additives in order to achieve high efficiency [54]. However, in our case, the presence of basic sites (due to Cs ions incorporation) in the meso Cs/MnO_x material promoted the esterification reaction. This can be supported by higher activity (>99%) of meso Cs/MnO_x compare to meso MnO_x (72%) in oxidative esterification of 1-octanol. Both materials were prepared by same synthesis procedure and presented monomodal mesoporous size distribution. The surface area of meso MnO_x material (200 $m^2\,g^{-1}$) is higher than meso Cs/MnO_x material (79 $m^2\,g^{-1}$). Therefore, the presence of basic sites in the meso Cs/MnO_x material is the predominant factor for higher activity in these esterification reactions.

Formation of esters with their acidic part bearing less carbons than the parent alcohol indicates a decarboxylation mechanism [55]. To form fewer esters, we selected solvent free oxidation of 2-phenylethanol (one aliphatic CH_2 group) for the mechanistic investigation. The oxidation of 2-phenylethanol leads to phenethyl benzoate (the acidic part of the ester has one less carbon than the parent alcohol) as the only ester. We used temperature programmed desorption (TPD) of the used catalyst to detect the CO_2 probably due to decarboxylation of the 2-phenylethanoic acid (by oxidation of 2-phenylethanol). To compare, the bare catalyst and the catalyst after adsorption of 2-phenylethanol at room temperature were also tested for CO_2-TPD (Fig. S12). The used catalyst displayed two desorption peaks of CO_2 at 340 °C and 500 °C respectively, whereas no CO_2 desorption was observed for the bare catalyst. On the other hand, the treated catalyst after adsorption displayed only one peak at 335 °C. Based on these observations, we propose an oxidation-decarboxylation-oxygen rebound mechanism [56]. The ester production was initiated by the oxidation of alcohol to acid, followed by a decarboxylation with a subsequent oxygen rebound mechanism by a radical intermediate, which generated an aldehyde having one carbon less than the parent alcohol (Schemes S3 and S4). Formation of a trace amount of benzaldehyde and inhibition of reaction by addition of a radical inhibitor (phenothiazine) support our mechanism. The aldehyde was further reacted with the alcohol to yield the desired ester, promoted by the basic nature of meso Cs/MnO_x [40].

5. Conclusion

In conclusion, we demonstrated meso Cs/MnO_x as a multifunctional catalyst for versatile tandem oxidation processes. This material was found to be efficient in catalyzing different mechanistically distinct reactions in one-pot under aerobic conditions. Seven different functional moieties can be evolved from a single substrate (alcohol) by using a single catalyst. Moreover, for the first time we observed multiple esterification from a single alcohol by a single catalyst under aerobic atmospheric conditions. The observed catalysis was truly heterogeneous and the catalyst can be reused without any loss of catalytic performance. Our catalytic protocol provides a new route for sustainable tandem oxidation processes by using an inexpensive material.

Acknowledgements

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.apcatb.2016.10.061.

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